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Application Serial No.: 10/045,360

Response dated May 10, 2004

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This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended) A method for determining steroid responsiveness in a subject, the

method comprising the steps of:

(a) obtaining a tissue, body fluid or cell sample from a subject undergoing steroid

treatment;

(ab) determining a first level of expression of RNA from a first gene known or suspected

to be steroid responsive in a tissue, body fluid or cell from a subject undergoing steroid

treatment;

(be) determining a second level of expression of RNA from a second gene known or

suspected to be non-responsive to steroids in the tissue, body fluid or cell; and

(cd) comparing the first and second levels of RNA to create a ratio;

(d) determining the steroid responsiveness of the subject based on the ratio, wherein the

subject is steroid responsive if the ratio is higher than a predetermined control ratio for

untreated or nonresponsive subjects, or similar to prior ratios for the subject when the subject

was previously determined to be responsive.

Claim 2 (currently amended) A method for determining steroid responsiveness in a tissue, body

fluid or cell, the method comprising the steps of:

(a) exposing a tissue, body fluid or cell sample in vitro to a steroid;

(b) determining a first level of expression of RNA from a first gene known or suspected

to be steroid responsive;

(c) determining a second level of expression of RNA from a second gene known or

suspected to be non-responsive to steroids; and

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(d) comparing the first and second levels of RNA to create a ratio;

(e) determining the steroid responsiveness of the tissue, body fluid or cell based on the ratio, wherein the tissue, body fluid or cell sample is steroid responsive if the ratio is higher than a predetermined control ratio for untreated or nonresponsive subjects, or similar to prior ratios for the subject when the subject was previously determined to be responsive.

Claim 3 (currently amended) A method for determining steroid responsiveness in a subject, the method comprising the steps of:

- (a) obtaining a pre-treatment tissue, body fluid or cell from a subject;
- (ab) determining a level of expression of an RNA expressed in the pre-treatment tissue, body fluid or cell-from a first gene known or suspected to be responsive to steroids in a pre-treatment tissue, body fluid, or cell from a subject;
- (<u>be</u>) determining a level of <u>expression of an RNA expressed in the pre-treatment tissue</u>, body fluid or cell-from a second gene known or suspected to be un-responsive to steroids <u>in</u> the pre-treatment tissue, body fluid, or cell;
 - (d) administering a steroid to the subject;
- (e) obtaining a post-treatment tissue, body fluid or cell from the subject after steroid administration;
 - $(\underline{c}f)$ determining a post-treatment level of RNA expressed from the first gene;
 - (dg) determining a post-treatment level of RNA expressed from the second gene;
- (eh) comparing the pre-treatment level of RNA expressed from the first gene to the pretreatment level of RNA expressed from the second gene to create a first normalized value;
- (if) comparing the post-treatment level of RNA expressed from the first gene to the post-treatment level of RNA expressed from the second gene to create a second normalized value;
 - (jg) comparing the first normalized value to the second normalized value;

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(h) determining steroid responsiveness of the subject based upon the comparison of the first normalized value to the second normalized value, wherein if the first normalized value is less than the second normalized value, it is indicative of steroid responsiveness in the tissue, body fluid or cell, and/or if the first normalized value is greater than or the same as the second normalized value, it is indicative of steroid non-responsiveness in the cell, and/or wherein the difference between the first normalized value and the second normalized value

Claim 4 (currently amended) A method for determining an effective dose of a steroid in a subject, the method comprising the steps of:

- (a) administering to a subject a dose of a steroid;
- (b) obtaining a\tissue, body fluid or cell from the subject;

correlates to the ability of the subject to respond to the steroid.

- (<u>be</u>) determining a first level of expression of RNA from a first gene known or suspected to be steroid responsive <u>in a tissue</u>, <u>body fluid</u>, <u>or cell from the subject</u>;
- (<u>c</u>d) determining a second level of expression of RNA from a second gene known or suspected to be non-responsive to steroids in the tissue, body fluid, or cell; and
 - (de) comparing the first and second levels of RNA to create a ratio;
- (e) determining the effective dose of the steroid in the subject based on the ratio, wherein the difference between the first RNA level and the second RNA level is indicative of the effectiveness of the steroid dose in the subject.

Claim 5 (currently amended) A method for monitoring a subject's ability to respond to a steroid, the method comprising the steps of:

- (a) administering to a subject a dose of steroid;
- (b) obtaining a tissue, body fluid or cell from the subject;

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(eb) determining a first level of expression of RNA from a first gene known or suspected to be steroid responsive in a tissue, body fluid, or cell from the subject;

- (dc) determining a second level of expression of RNA from a second gene known or suspected to be non-responsive to steroids in the tissue, body fluid, or cell; and
 - (ed) comparing the first and second levels of RNA to create a ratio;
- (e) monitoring the subject's ability to respond to the steroid based upon the ratio, wherein the subject is steroid responsive if the ratio is higher than a predetermined control ratio for untreated or nonresponsive subjects, or similar to prior ratios for the subject when the subject was previously determined to be responsive.

Claim 6 (currently amended) A method for determining drug responsiveness in a subject undergoing drug treatment, the method comprising the steps of:

- (a) obtaining a tissue, body fluid or cell from a subject undergoing treatment with a drug;
- (<u>ab</u>) determining a first level of expression of RNA from a first gene known or suspected to be drug-responsive in a tissue, body fluid, or cell from a subject undergoing treatment with a drug;
- (<u>be</u>) determining a second level of expression of RNA from a second gene known or suspected to be non-responsive to the drug in the tissue, body fluid, or cell; and
 - (cd) comparing the first and second levels of RNA to create a ratio;
- (d) determining drug responsiveness in the subject undergoing drug treatment based upon the ratio, wherein the subject is drug-responsive if the first level is higher than the second level and the subject is non-responsive to drug if the second level is higher than the first level.

Claim 7 (currently amended) A method for determining drug responsiveness in a tissue, body fluid or cell, the method comprising the steps of:

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- (a) obtaining a tissue, body fluid or cell;
- (<u>ab</u>) exposing the <u>a</u> tissue, body fluid or cell in vitro to a drug;
- (eb) determining a first level of expression of RNA from a first gene known or suspected to be drug-responsive;
- (dc) determining a second level of expression of RNA from a second gene known or suspected to be non-responsive to the drug; and
 - (ed) comparing the first and second levels of RNA to create a ratio;
- (e) determining drug responsiveness in the tissue, body fluid, or cell based upon the ratio, wherein the tissue, body fluid or cell is drug-responsive if the first level is higher than the second level and the tissue, body fluid or cell is non-responsive to the drug if the second level is higher than the first level.

Claim 8 (previously presented) The method of claim 1, wherein one or more of the determining steps requires amplification of the RNAs.

Claim 9 (previously presented) The method of claim 8, wherein one or more of the determining steps requires polymerase chain reaction (PCR) of the RNAs.

Claim 10 (previously presented) The method of claim 1, wherein one or more of the determining steps requires *in situ* detection of the first and second RNA.

Claim 11 (currently amended) The method of claim 1, wherein one or more of the determining steps requires direct probing of the RNAs.

Claim 12 (currently amended) The method of claim 1, further comprising monitoring or tracking the steroid responsiveness over time to detect a change in steroid responsiveness.

Claim 13 (previously presented) The method of claim 1, further comprising the step of administering one or more pro-inflammatory and/or anti-inflammatory mediators to the tissue, body fluid or cell.

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Claim 14 (previously presented) The method of claim 13, wherein the pro-inflammatory mediator is selected from the group consisting of interleukin 1α (IL- 1α), interleukin- 1β (IL- 1β), interleukin 6 (IL-6), and tumor necrosis factor (TNF- α).

Claim 15 (previously presented) The method of claim 13, wherein the anti-inflammatory mediator is selected from the group consisting of interleukin 1 receptor antagonist (IL-1RA), tumor necrosis factor receptor antagonist (TNF-RA) or derivatives thereof, soluble TNF receptors, anti-TNF antibodies, and anti-TNF-RA antibodies.

Claim 16 (previously presented) The method of claim 1, further comprising the step of administering one or more cytokines, chemokines, interferons or hormones to the tissue, body fluid or cell.

Claim 17 (previously presented) The method of claim 16, wherein the chemokine is selected from the group consisting of interleukin-8 (IL-8).

Claim 18 (withdrawn)

Claim 19 (previously presented) The method of claim 1, wherein the tissue comprises blood.

Claim 20 (previously presented) The method of claim 1, wherein the tissue comprises nucleated cells.

Claim 21 (previously presented) The method of claim 1, wherein the cell is selected from the group consisting of a monocyte, a macrophage, a neutrophil, a T-cell, a B-cell, a basophil, a fibroblast, an endothelial cell and an epithelial cell.

Claim 22 (previously presented) The method of claim 1, wherein the tissue comprises buccal cells.

Claim 23 (previously presented) The method of claim 1, wherein the tissue comprises a biopsy sample.

Claim 24 (previously presented) The method of claim 1, wherein the tissue sample is stored in a stabilization solution prior to analysis.

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Claim 25 (previously presented) The method of claim 1, wherein the tissue sample is stored

frozen.

Claim 26 (previously presented) The method of claim 1, wherein the first gene encodes

serum amyloid A1 (SAA1).

Claim 27 (previously presented) The method of claim 1, wherein the second gene encodes

serum amyloid A2 (SAA2).

Claim 28 (previously presented) The method of claim 1, wherein the first gene or second gene encodes a chemokine, a cytokine agonist, a cytokine antagonist, or a complement

component.

Claim 29 (previously presented) The method of claim 1, further comprising the step of quantifying the RNA level of a third gene and comparing the RNA level from the third gene to the RNA level from the first gene and the RNA level from the second gene.

Claim 30 (previously presented) The method of claim 29, wherein the third gene encodes an acute phase reactant.

Claim 31 (previously presented) The method of claim 29, wherein the third gene encodes a chemokines, cytokine agonist, a cytokine antagonist, or a complement component.

Claim 32 (withdrawn)

Claim 33 (previously presented) The method of claim 1, wherein the subject suffers from an inflammatory condition, a disease with an inflammatory component, a disease with an inflammatory consequence, and/or a disease with inflammatory symptoms.

Claim 34 (withdrawn)

Claim 35 (previously presented) The method of claim 1, wherein the subject may be refractory, less responsive, or more responsive to steroid treatment.

Claim 36 (withdrawn)

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Claim 37 (withdrawn)

Claim 38 (previously presented) The method of claim 1, wherein the subject is steroid

dependent.

Claim 39 (previously presented) The method of claim 1, wherein the subject suffers from an

arthritic disease.

Claim 40 (currently amended) The method of claim 39, wherein the arthritic disease is selected from the group consisting of osteoarthritis, rheumatoid arthritis, psoriatic thoriatic arthritis or and idiopathic arthritis.

Claims 41 to 49 (withdrawn)

Claim 50 (previously presented) The method of claim 1, wherein the first gene is controlled by a steroid responsive element.

Claim 51 (previously presented) The method of claim 50, wherein the steroid responsive element is a glucocorticoid responsive element (GRE).

Claim 52 (previously presented) The method of claim 51, wherein the GRE is a consensus GRE or a non-consensus GRE.

Claim 53 (previously presented) The method of claim 52, wherein the consensus GRE is GGTACAnnnTGTTCT or a variation thereof, where n is any nucleotide.

Claim 54 (previously presented) The method of claim 1, wherein the second gene is encoded by a gene which is not controlled by a steroid response element.

Claim 55 (currently amended) The method of claim 1, wherein the steroid is <u>selected from</u> the group consisting of a glucocorticoid, an estrogen, or and an androgen.

Claim 56 (withdrawn)

Claim 57 (withdrawn)

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Claim 58 (currently amended) The method of claim 1, wherein the steroid is selected from the group consisting of alclometasone diproprionate, amcinonide, beclomethasone diproprionate, betamethasone, betamethasone benzoate, betamethasone diproprionate, betamethasone sodium phosphate, betamethasone sodium phosphate and acetate, betamethasone valerate, clobetasol proprionate, clocortolone pivalate, cortisol (hydrocortisone), cortisol (hydrocortisone) acetate, cortisol (hydrocortisone) butyrate, cortisol (hydrocortisone) cypionate, cortisol (hydrocortisone) sodium phosphate, cortisol (hydrocortisone) sodium succinate, cortisol (hydrocortisone) valerate, cortisone acetate, desonide, desoximetasone, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, diflorasone diacetate, fludrocortisone acetate, flunisolide, fluocinolone acetonide, fluocinonide, fluorometholone, flurandrenolide, halcinonide, medrysone, methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate. mometasone furoate, paramethasone acetate, prednisolone, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetonide, triamcinolone diacetate, and triamcinolone hexacetonide, or a synthetic analog thereof, or a combination thereof.

Claim 59 (previously presented) The method of claim 1, wherein the steroid is administered parenterally, orally or locally.

Claim 60 (previously presented) The method of claim 1, wherein the steroid is administered intravenously, intramuscularly, enterally, transdermally, nasally, transmucosally, via inhilation, and/or subcutaneously.

Claim 61 (withdrawn)

Claim 62 (withdrawn)